
Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

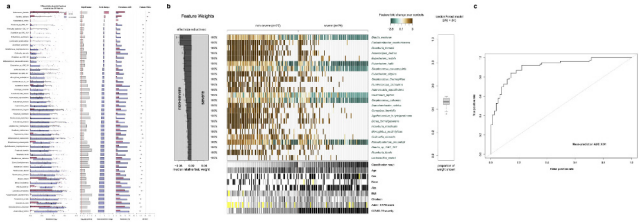

**Fig. 1. (A)** Using unsupervised feature selection (species abundance > 0.001) inclusive of taxa differentially abundant by non-parametric Wilcoxon rank-sum testing (nominal p-value < 0.05), **(B)** we performed random forest classification using a twice-repeated 5-fold cross-validation scheme to predict COVID-19 disease severity from shotgun metagenomic stool profiles **(C)** yielding an AUROC of 0.91.

**1165**

**SARS-COV-2 VACCINATION INDUCES A PREDOMINENTLY CLASS II (CYTOKINE EFFECTOR) T CELL RESPONSE, BUT THE CLASS I RESPONSE IS AUGMENTED BY ANTI-TNF THERAPY AND VACCINE TYPE**

Alexander Xu, Dalin Li, Rebecca Elyanow, Rachel M. Gittelman, Heidi Chapman, John Prostko, Valeriya Pozdnyakova, Philip Debbas, Angela Mujukian, Arash A. Horizon, Kimia Sobhani, Susan Cheng, Ian M. Kaplan, Dermot P.B. Mcgovern, Akil Merchant, Gil Melmed, Jonathan G. Braun

**BACKGROUND**: In response to COVID-19 vaccination, cytotoxic and cytokine effector T cell immune responses are elicited in the T-cell compartment, based on recognition of epitopes presented by Class I or Class II MHC molecules, respectively. The levels of these distinct T-cell responses may have significant implications for immunization strategies and risk assessment. Knowledge of these two responses after vaccination is still largely unknown, especially in the context of immunomodulatory treatment regimens. **METHODS**: We performed T-cell receptor (TCR) immunosequencing (Adaptive Biotechnologies, Seattle WA) of IBD patients (N=303) and health care worker controls (HCW, N=224) at up to four time points (prior to dose 1, prior to dose 2, 2 weeks after dose 2, 8 weeks after dose 2). Two metrics of TCR response, breadth (# of unique antigen-specific sequences) and depth (expansion of antigen-specific sequences), were calculated for all sequences and Class I- and Class II-specific sequences, and compared to demographics, IBD treatment, and vaccine type. Subjects with exceptional Class I or Class II responses were calculated as significant residuals relative to the Class I vs. Class II regression line. Similar associations were observed for both breadth and depth: breadth is presented here for brevity. **RESULTS**: Both Class I- and Class II-specific T-cell responses peaked 2 weeks after dose 2, and significantly correlated with lower age, female gender, and mRNA vaccine type (mRNA-1273/Moderna and BNT262b/Pfizer, versus vector vaccine AD26CoV2/J&J) (FIGURE). Class II responses comprised ~85% of detected TCR response in both IBD and HCW subjects. Among IBD patients, there was a significant elevation of the class I response with anti-TNF treatment (p=0.04). This effect was most pronounced at later timepoints, suggesting that anti-TNF permitted a more persistent Class I-specific response. Among patients with exceptionally high or low Class I TCR response, there were significant differences in TCR metrics across vaccine types (p=0.0035). 21% of AD26CoV2 patients were highly Class I-biased (Zscore>1, 9.4% and 7.3% for BNT162 and mRNA-1273, respectively), and this was correlated with lower anti-spike serology 2 and 8 weeks after vaccination (p<1E-10). Conversely, mRNA-1273 patients were Class I-deficient, representing 25.3% of patients but 44.1% of highly Class I-deficient patients (Zscore<1, 0% for AD26CoV2). **CONCLUSION**: The T-cell clonal response to SARS-CoV-2 vaccine is Class II-predominant, but the Class I-response is augmented by anti-TNF therapy and vector vaccine type. These factors may help guide reimmunization vaccine strategy in immune-impaired populations, and warrant further study of the effects of anti-TNF therapies on vaccine efficacy.

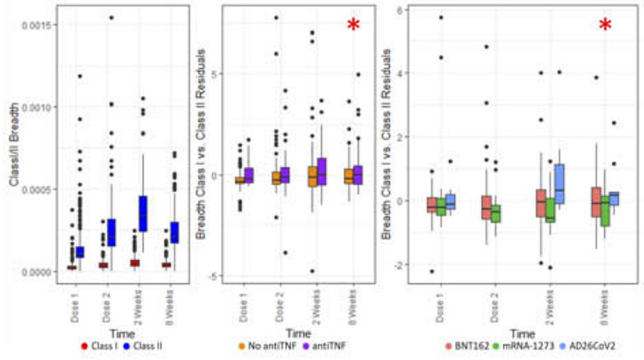


**Figure**: TCR response time course (left); effect of anti-TNF (middle); effect of vaccine type (right). Breadth was predominantly Class II for most patients, with maximum response at 2 weeks after full vaccination (left). The balance of Class I vs. Class II response was significantly biased towards Class I at 8 weeks after full vaccination for patients receiving anti-TNF treatment for IBD (asterisk, p=0.036). Patients receiving AD26CoV2 vaccines were significantly increased in Class I responses, while patients receiving mRNA-1273 vaccines were significantly reduced for Class I responses (t-tests: p=0.0036 at 8 weeks [asterisk], p=0.051 at 2 weeks).

**1166**

**IN-PATIENT ANTIBIOTIC EXPOSURE PROMOTES SARS-COV-2 PERSISTENCE IN THE GI TRACT IN COVID-19 ADMITTED PATIENTS**

Ashok Sharma, Anthony Martin, Jacob E. Moskowitz, Stephanie Bora, Katherine Legree, Pieter Dorrestein, David Underhill, Rob Knight, Peter Chen, Suzanne Devkota

**Background:** SARS-COV-2 shedding in the stool long after clearance from the respiratory tract has been reported in several studies during the COVID-19 pandemic. This suggests a long tail of viral persistence in the GI tract even after a patient has tested negative via oro-nasal swabs. Most patients admitted to the ICU or wards for COVID-19 at Cedars-Sinai are placed on between 2-13 antimicrobials at admission in order to prevent secondary respiratory infections, leading us to question whether the effect of reducing or eliminating the gut microbiome during SARS-COV-2 infection may result in prolonged GI infection and long-term GI side-effects. Antibiotic pre-treatment in rodent studies has shown that flaviviruses persist longer in the GI tract in the absence of gut microbiota. Studies have also demonstrated that antibiotic pre-treatment attenuates the antibody responses to the flu vaccine in mice and humans. Collectively, this suggests a reduction or elimination of the gut the microbiota by antibiotics before or during viral infection can drive viral persistence in the GI tract. **Methods:** Longitudinal stool samples were collected from 29 COVID-19 in-patients (wards, n=12; ICU, n=17, n=79 stool samples total) and 9 non-COVID-19 in-patients admitted for other respiratory infections. Ten of 29 COVID-19 in-patients were antibiotic naive. Stool metagenomics, metabolomics, and SARS-COV-2 viral quantification by qPCR, and fecal calprotectin were measured and aligned with antibiotic exposure of each patient. **Results:** Our findings show that 72% of stool samples from COVID-19 patients that tested negative for SARS-COV-2 in the stool were never exposed to in-patient antibiotics. Fecal calprotectin was significantly higher in ICU-admitted COVID-19 patients compared to those in the wards and non-COVID-19 controls. The highest fecal calprotectin levels corresponded to nine samples from three ICU patients, all of whom were on the heaviest regimen of antibiotics and were positive for SARS-COV-2 in the stool. Expectedly, gut microbiota variance was explained largely by antibiotic status, but also independently by stool SARS-COV-2 status. We recruited an additional 34 patients during the delta variant surge, and these samples are currently being analyzed along with fecal metabolomics. **Conclusion:** The heavy-dose antibiotic regimen administered to COVID-19 in-patients is associated with viral persistence of SARS-COV-2 in the GI tract, suggesting an important role of the gut microbiome in excluding SARS-COV-2 from the GI tract, perhaps by competitive exclusion or promoting interferon responses. Intestinal inflammation was significantly greater in COVID-19 ICU patients, with the highest levels of fecal calprotectin correlating to the heaviest dose of antibiotics and presence of SARS-COV-2 in the stool.

**Sa1000**

**DIARRHEA, ELEVATED AST, AND ELEVATION OF INFLAMMATORY-RELATED BIOMARKERS IS A PREDICTOR FOR MORTALITY IN MINORITY HOSPITALISED COVID-19 PATIENTS**

Hassan Ashktorab, Antonio Pizuorno, Folake O. Adeleye, Adeyinka O. Laiyemo, Maryam Mehdipour Dalivand, Farshad Aduli, Zaki A. Sherif, Gholamreza Oskrochi, Kibreab Angesom, Philip Oppong-Twene, Suryanarayana Reddy Challa, Nnaemeka C. Okorie, Esther S. Moon, Edward L. Ramos, Boubini Jones-Wonni, Abdoul M. Kone, Sheldon Rankine, Camelita Thrift, Chiamaka C. Ekwunazu, Derek Scholes, Abigail Banson, Brianna Mitchell, Guttu Maskalo, Jillian D. Ross, Julencia Curtis, Rachel Kim, Chandler Gilliard, Geeta Ahuja, Joseph Mathew, Warren Gavin, Areeba Kara, Manuel Hache-Marliere, Leonidas Palaiodimos, Vishnu R. Mani, Aleksandr Kalabin, Vijay Gayam, Pavani Garlapati, Joseph Miller, Lakshmi G. Chirumamilla, Faezeh Ahangarzadeh, Bahador Bina, Fatimah L. Jackson, John M. Carethers, Farin Kamangar, Hassan Brim

**Background and Aims:** Initial reports on US COVID-19 showed different outcomes in different races. In this study, we use a diverse large cohort of hospitalized COVID-19 patients to determine predictors of mortality. **Methods:** We analyzed data from hospitalized COVID-19 patients (n=5,852) from 8 hospitals. Demographics, comorbidities, symptoms and laboratory data were collected. **Results:** The cohort contained 3,662 (61.7%) African Americans (AA), 286 (5%) American Latinx (LAT), 1,407 (23.9%), European Americans (EA), and 93 (1.5%) American Asians (AS). Survivors and dead patients' mean ages were 58 and 68 for AA, 58 and 77 for EA, 44 and 61 for LAT, and 51 and 63 for AS. Mortality rates for AA, LAT, and EA were 14.8%, 7.3%, and 16.3%. Mortality increased among patients with the following characteristics: age, male gender, New York region, cardiac disease, COPD, diabetes mellitus, hypertension, history of cancer, immunosuppression, elevated lymphocytes, CRP, ferritin, D-Dimer, creatinine, troponin, and procalcitonin. Use of mechanical ventilation, respiratory failure, shortness of breath (SOB) (p<0.01), fatigue (p=0.04), diarrhea (p=0.02), and increased AST (p<0.01), significantly correlated with death in multivariate analysis. Male sex and EA and AA race/ethnicity had a higher frequency of death. Diarrhea was among the most common GI symptom amongst AAs (6.8%). When adjusting for comorbidities, significant variables were age (over 45 years old), male sex, EA, patients hospitalized in Indiana, Michigan, Georgia, and District of Columbia. When adjusting for disease severity, significant variables were age over 65 years old, male sex, EA as well as having SOB, elevated CRP, and D-dimer. Glucocorticoid usage was associated with an increased risk of COVID-19 death in our cohort. **Conclusion:** Among this large cohort of hospitalized COVID-19 patients enriched for African Americans, predictors of mortality include male gender, diarrhea, elevated AST, comorbidities, respiratory symptoms and failure, and elevation of inflammatory-related biomarkers. These findings may reflect the extent of systemic organ involvement by SARS-CoV-2 and subsequent progression to multi-system organ failure. High mortality in AA in comparison with LAT is likely related to a high frequency of comorbidities and older age among AA.